IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BRIGHAM AND WOMEN'S HOSPITAL INC., et al.	:	CIVIL ACTION
v.	:	
TEVA PHARMACEUTICALS USA, INC., et al.	:	NO. 08-464

MEMORANDUM, INCLUDING
FINDINGS OF FACT
AND CONCLUSIONS OF LAW

Bartle, C.J. January 7, 2011

Plaintiffs Brigham and Women's Hospital, Inc. ("BWH"), NPS Pharmaceuticals, Inc. ("NPS"), and Amgen Inc. ("Amgen") (collectively "plaintiffs") filed suit against Teva Pharmaceuticals USA, Inc. ("Teva USA"), Teva Pharmaceutical Industries Ltd. ("Teva"), and Barr Laboratories, Inc. ("Barr") (collectively "defendants") for infringement of four pharmaceutical patents.[1] These patents, U.S. Patent Nos. 6,011,068 (the "'068 patent"), 6,031,003 (the "'003 patent"), 6,211,244 (the "'244 patent"), and 6,313,146 (the "'146 patent"), each state claims relating to the production and/or medicinal use of cinacalcet hydrochloride ("cinacalcet"), a compound Amgen sells under the trade name Sensipar. Pursuant to a stipulation by the parties, the court subsequently dismissed all claims and counterclaims pertaining to the '146 patent.

1. On December 23, 2008, after the beginning of litigation, Teva USA acquired Barr. Barr is now a wholly-owned subsidiary of Teva USA.

Given the large number of patent claims potentially implicated by the plaintiffs' complaint, the court ordered the plaintiffs to select representative claims for trial. Plaintiffs elected to proceed on claims 5 and 26 of the '244 patent; claims 7, 32, 74, and 84 of the '068 patent; and claims 19, 45, 82, 89, 115, and 145 of the '003 patent. Prior to litigation, both Teva USA and Barr filed Abbreviated New Drug Applications ("ANDAs") with the Food and Drug Administration ("FDA") in which they sought permission to produce and sell a product containing cinacalcet. Defendants thereafter stipulated that the cinacalcet product they contemplated selling, as set forth in their ANDAs filed with the FDA, would infringe each of the representative claims.

The gravamen of the action now revolves around defendants' assertion that the '068, '003, and '244 patents are invalid. They assert that the '068 and '003 patents are invalid due to plaintiffs' inequitable conduct during prosecution of the applications for those two patents before the U.S. Patent and Trademark Office ("PTO") and that both the '068 and '003 patents impermissibly double patent claims in the '244 patent.

Defendants also maintain that the '244 patent is unenforceable because it was anticipated by U.S. Patent No. 5,648,541 ("'541 patent")[2] and because plaintiffs engaged in

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2. At trial, defendants abandoned their contention that the '146 patent anticipates the '244 patent.

inequitable conduct before the PTO during prosecution of the application for the '244 patent.

Following a three-day bench trial, the court makes the following findings of fact and conclusions of law.

I.

Cinacalcet, the active ingredient in Sensipar, mimics the effects of calcium ions in the human body. Accordingly, cinacalcet belongs to a class of compounds known as "calcimimetics." Cinacalcet "mimics" calcium ions in the sense that it increases the parathyroid gland's sensitivity to such ions in the blood.[3] In 2004, the FDA approved cinacalcet as a method of treating patients with parathyroid carcinoma and secondary hyperparathyroidism, conditions in which the parathyroid gland's response to calcium ions is diminished. Currently, there are no other calcimimetic compounds approved by the FDA to treat these maladies.

In 1993, plaintiff NPS began collaborating with plaintiff BWH on this calcimimetic research. In 1996, NPS entered into an agreement with plaintiff Amgen to develop and market a calcimimetic pharmaceutical product from among the 500 to 600 compounds NPS has created as part of its research. Of the compounds Amgen selected and tested, cinacalcet emerged as the compound with the greatest pharmaceutical promise.

The chemical structure of cinacalcet is as follows:

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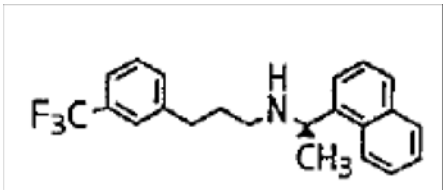
3. Other calcimimetic drugs actually "mimic" calcium ions. Cinacalcet does not.



The hexagonal shape at the left side of the compound is a phenyl ring. The "F_3C" is a trifluoromethyl and is in the phenyl ring's meta position. Moving to the right, the "CH_3" is a methyl group, and the vertically-stacked hexagons at the far right are known as a "1-napthyl," which is two fused benzene rings. The solid triangle immediately above the methyl group signifies that this compound is an "R-enantiomer," meaning that the methyl group extends from the plane of the page toward the viewer.[4]

NPS's calcimimetic research spawned many patents and patent applications. NPS filed the '068 application[5] on December 8, 1994 as a continuation-in-part application in a long series of continuation applications dating back to August 23, 1991. The '068 patent issued on January 4, 2000 and will expire on December 14, 2016. This expiration date reflects a terminal disclaimer plaintiffs executed in the '068 prosecution to make

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4. In stereochemistry, an enantiomer describes a compound with a specific orientation in three-dimensional space. An R-enantiomer is a component extending from the plane of the page to the viewer, while an S-enantiomer is a component extending behind the plane of the page. The important feature of R- and S-enantiomers is that, like the right and left human hands, they are not superimposable.

5. The application that issued as the '068 patent was numbered 08/353,784. For clarity, we will follow the parties' practice of referring to an application by the same three numbers as the patent that ultimately issued from that application.

that patent's expiration coterminous with U.S. Patent No. 6,001,884 ("'884 patent").[6] Like the '068, '003 and '244 patents, the '884 patent states claims related to calcimimetic compounds and is assigned to NPS.

Claims 7 and 32 of the '068 patent both describe genera of compounds and the pharmaceutically acceptable acid addition salts and complexes of those compounds. Claim 74 teaches the property of causing an increase in calcium ions in bovine parathyroid cells at a particular concentration of a genus of compounds. Similarly, claim 84 describes a pharmaceutically acceptable composition of a group of compounds. It is undisputed that cinacalcet is a species compound within the genus described in claim 7 of the '068 patent.

Plaintiffs filed the '003 and '146 patent applications (respectively, applications 08/484,719 and 08/484,159) on June 7, 1995 as continuation-in-part applications of the '068 application. The '003 patent issued on February 29, 2000, and the '146 patent did so on November 6, 2001. Like the '068 patent, both the '003 and '146 patents expire on December 14, 2016. Generally, the '003 patent claims methods of treating patients, including patients with thyroid conditions, using

6. During trial, plaintiffs informed the court that the PTO had granted plaintiffs' request to extend the term of the '068 patent 449 days from December 14, 2016 pursuant to 35 U.S.C. § 156. See Merck & Co., Inc. v. Hi-Tech Pharmacal Co., Inc., 482 F.3d 1317, 1320-21 (Fed. Cir. 2007).

calcimimetic compounds with a chemical structure similar to the compounds described in the '068 patent.[7]

As noted above, the '003 and '146 applications were filed on June 7, 1995. This was the last day before a significant change in the term of patents became effective as a result of legislation conforming to a treaty to which the United States is a party. Patents awarded on applications pending as of June 7, 1995, such as the '068, '003, and '146 applications, were eligible to receive terms for the longer of either 17 years from the date of issue or 20 years from the date the application was filed.[8] Patents granted on applications filed on or after June 8, 1995 receive terms of 20 years from the date of the application's filing. 35 U.S.C. § 154; see Uruguay Round Agreement Act, Pub. L. No. 103-465, 108 Stat. 4809, 4983 (1994), amending 35 U.S.C. § 154; DuPont Merck Pharm. Co. v. Bristol-Myers Squibb, Co., 62 F.3d 1397, 1398-1400 (Fed. Cir. 1995). Significantly, this change created the possibility that a patent granted on an application filed before June 8, 1995 have a longer term than an application filed on June 8, 1995 or thereafter. This result would occur if the pre-June 8, 1995 application was delayed in issuing as a patent for more than three years.

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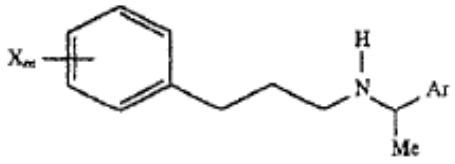
7. The '146 patent claims a genus of organic compounds and pharmaceutical compositions of those compounds.

8. Similarly, the legislation provided that the term of any patent scheduled to expire on or after June 8, 1995 would also have a term of 20 years from application or 17 years from issue, whichever was longer. 35 U.S.C. § 154(c)(1).

Plaintiffs filed the '541 application (application 535,469) on September 28, 1995. The PTO granted the patent on July 15, 1997. Since the application was filed after June 7, 1995, the patent is scheduled to expire on September 28, 2015, twenty years after the application was filed.

The '541 patent describes a process for creating the R-enantiomer of a genus of compounds. Claim 1 of the '541 patent is broadest and describes a process for creating an excess of R-enantiomers of compounds with the following basic structure:



Claim 1 describes three possible substituents for the right-side "Ar" component and 22 possible substituents for left-side X_m component.[9] Additionally, "m" must be an integer between 1 and 5, which means that between one and five of the possible X substituents may be joined to the left side of the molecule. Mathematically, claim 1 describes at least 160×10^{12} compounds.[10] It is undisputed that cinacalcet is one such compound.

The '541 patent's specification discloses that the process described can be used to create fifteen preferred R-

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9. This excludes one possible X substituent, lower alkyl, which testimony elicited at trial demonstrated could appear in this molecule in at least six different permutations.

10. No evidence demonstrated whether each of the mathematically possible combinations of substituents is chemically attainable.

enantiomer compounds, including two "most preferred" compounds. Each preferred compound has a 3-methoxyphenyl as the "Ar" component at the right side of the compound. The variation among the '541 patent's preferred compounds exists exclusively in the left-side X_m component. One of the X_m components the '541 patent describes as "preferred" is CF_3, the same substituent that exists at the left-most end of cinacalcet.

On October 23, 1995, NPS filed the '244 application (number 08/546,998), which issued on April 3, 2001. Again, since the application was filed after June 7, 1995, the patent will expire on October 23, 2015, twenty years from the application date. The '244 patent claims a number of specific compounds and medicinal uses of those compounds. Representative claim 5 of the '244 patent claims cinacalcet and pharmaceutically acceptable salts made from cinacalcet. Claim 26 claims a method of using cinacalcet to decrease a patient's parathyroid hormone to achieve a beneficial effect.

The '068, '003, '146, and '244 patents were prosecuted primarily by four attorneys: Dr. Frank Ungemach, James Jensen, Dr. Richard Warburg, and Dr. Sheldon Heber (collectively the "patent committee"). Drs. Heber and Warburg were attorneys at Lyons & Lyons, the law firm NPS and Amgen retained as outside counsel for these prosecutions. Dr. Ungemach was an attorney employed by Amgen, and Jensen was NPS's in-house counsel.

The named inventors as well as the prosecuting attorneys are required to disclose to the PTO information

material to those prosecutions under 37 C.F.R. § 1.56, an obligation referred to as a "duty of candor." During the time period at issue, § 1.56 defined "material" information as follows:

> Under this section, information is material to patentability when it is not cumulative to information already of record or being made of record in the application, and
> (1) It establishes, by itself or in combination with other information, a prima facie case of unpatentability of a claim; or
> (2) It refutes, or is inconsistent with, a position the applicant takes in:
> (i) Opposing an argument of unpatentability relied on by the Office, or
> (ii) Asserting an argument of patentability.
> A prima facie case of unpatentability is established when the information compels a conclusion that a claim is unpatentable under the preponderance of evidence, burden-of-proof standard, giving each term in the claim its broadest reasonable construction consistent with the specification, and before any consideration is given to evidence which may be submitted in an attempt to establish a contrary conclusion of patentability.

37 C.F.R. § 1.56.[11]

Amgen's internal documents reveal that developing marketable calcimimetic compounds was a high priority for the

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11. This definition of materiality became effective March 16, 1992. See Duty of Disclosure, 57 Fed. Reg. 2021 (Jan. 17, 1992). The Court of Appeals for the Federal Circuit has found, however, that the PTO's revised definition of materiality in § 1.56 did not alter the test to be applied in determining whether information was material for the purposes of an inequitable conduct analysis. Digital Control, Inc. v. Charles Mach. Works, 437 F.3d 1309, 1314-16 (Fed. Cir. 2006). That standard is discussed below.

company. It also forecasted that its sales of calcimimetic drugs would exceed $400 million in five years. Although Amgen's sales forecast proved prescient, there is no evidence that the patent committee knew of Amgen's priorities or predicted sales.

Unlike the '068, '146, '003 and '244 patent applications, the '541 patent application was prosecuted by the law firm of Trask, Britt & Rossa. The patent committee disclosed two calcimimetic-related patents prosecuted by Trask, Britt & Rossa during the '068 prosecution. Dr. Heber testified he was aware of one "process patent," which was never identified, related to calcimimetic compounds that was prosecuted by another law firm.

Defendants' assertions of inequitable conduct on the part of plaintiffs revolve around the prosecutions of the '068, '003, and '244 applications. The '068, '003, '146, and '244 applications were examined by four different PTO patent examiners. The parties acknowledge that the three examiners considering the '068, '003, and '146 applications were each aware of the other two applications because the '003 and '146 applications were filed as continuations-in-part applications of the '068 application.

On October 30, 1996, the examiner issued anticipation and obviousness rejections in the '244 application over ten prior art references. On April 30, 1997, the patent committee responded to the rejections by canceling certain claims, amending

some of the claims, and by arguing that three of the claims (as amended) were distinct from the prior art cited.

On June 5, 1997, the patent committee also submitted a supplemental information disclosure statement (IDS) to the '068 examiner. This IDS discloses 21 additional publications, 11 foreign patents, and two U.S. patents held by Dr. Van Wagenen that had been prosecuted by Trask, Britt & Rossa. Of the references disclosed in the IDS, eight are references cited by the '244 examiner in his October 30, 1996 rejection. The patent committee submitted the IDS with a cover letter stating these "patents and publications ... were recently cited by an examiner in a related application ...."

On October 28, 1997, the '068 examiner provisionally rejected numerous claims in the '068 application as obvious-type double patenting in light of the claims simultaneously pending in '146 application and the application that led to the '884 patent. This office action returned the June 5, 1997 IDS with the '068 examiner's initials next to each of the cited references. Then, on December 23, 1997, the '146 examiner provisionally rejected nearly all claims in the '146 application as obvious-type double patenting of claims in the '068 and '884 applications.

On March 2, 1998, the PTO issued a notice of allowance with regard to the '244 application. On May 14, 1998, Drs. Warburg and Heber requested a meeting with the patent committee to discuss "further prosecution" of the '244 application.

According to letters exchanged between committee members, a meeting was to occur on May 18, 1998 to discuss the '244 patent.

Following this meeting, on May 29, 1998, the patent committee filed a continuing prosecution application (CPA) in the '244 prosecution. The CPA also contained a disclosure statement on which the patent committee revealed to the '244 examiner the existence of the copending '068, '003, and '146 applications. A draft of the disclosure statement circulated among the committee members stated, "The enclosed CPA is being filed to ... inform the Examiner of the copending applications.... Applicants would like to bring to the Examiner's attention copending applications U.S. Serial Nos. 08/353,784, 08/469,204, and 08/484,159. These copending applications list common inventors with the present application." The CPA filed with the PTO omitted the first quoted sentence.

The '244 examiner did not issue any rejections based on the copending '068, '003, or '146 applications. The patent committee never informed the '244 examiner in the CPA or at any other time about the '541 application or patent.

While the patent committee disclosed the '068, '003, and '146 applications to the '244 examiner, it never mentioned to the '068, '146, or '003 examiners the existence of the '244 application or the rejections the '244 examiner made on October 30, 1996. The members of the patent committee do not recall, now some twelve years later, why the disclosure of the '068, '003, and '146 applications went only to the '244 examiner,

and not also vice versa. None of the four attorneys could specifically recall any discussions about what information should be disclosed in any of the prosecutions.

Nevertheless, two of the four attorneys testified they did not disclose the '244 application to the other three examiners because the '244 application was not prior art to those applications, that is, that the '244 application was filed after the '068 and '003 applications and was still pending when the '068 and '003 patents issued. Dr. Heber testified that the '244 application was not disclosed because it was not prior art and did not issue as a patent during prosecution of the other three applications. Dr. Ungemach testified that the patent committee did not need to disclose the '244 application because copending applications only had to be disclosed if they had an earlier priority date. Dr. Ungemach also testified that his view of the law in 1998 did not require disclosure of a later-filed application claiming a species compound, such as the '244 application, because that application could not be prior art to an earlier-filed application claiming the genus. The patent committee members all testified that it was their practice in 1998 to disclose all material information to the PTO.

Prior to their issuance as patents, the patent committee executed terminal disclaimers in the '068, '003, and '146 applications to disclaim any patent term beyond December 14, 2016. As noted above, these disclaimers made the '068, '003, and '146 patents coterminous with NPS's '884 patent.

Plaintiffs have listed the '068, '003, '146, and '244 patents in the FDA's Orange Book as stating claims that cover cinacalcet.[12] On June 16, 2008, plaintiffs received notice from Teva USA and Barr that each had filed an Abbreviated New Drug Application with the FDA regarding a product they intended to launch to compete with Sensipar. With regard to patents covering a proposed generic drug, each "ANDA applicant must certify that (i) no such patent information has been submitted to the FDA; (II) the patent has expired; (III) the patent is set to expire on a certain date; or (IV) the patent is invalid or will not be infringed by the manufacture, use, or sale of the new generic drug for which the ANDA is submitted." 21 U.S.C. § 355(j)(2)(A)(vii)(I-IV); see Andrx Pharm., Inc. v. Biovail Corp., 276 F.3d 1368, 1371 (Fed. Cir. 2002). This certification must be made for each patent listed in the FDA's Orange Book as claiming an approved drug. 21 U.S.C. § 355(j)(2)(A)(vii). As to the patents in suit, Teva USA and Barr's ANDAs contained "Paragraph IV" certifications. By statute, the ANDAs that Teva USA and Barr filed and served on plaintiffs are deemed acts of infringement allowing the patent-holder to initiate an

12. By statute, any person seeking FDA approval for a drug must notify the FDA of all patents "with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug." 21 U.S.C. § 355(b)(1). The FDA lists such patents in a volume called the Approved Drug Products With Therapeutic Equivalence Evaluations, more commonly known as the "Orange Book." See Andrx Pharm., Inc. v. Biovail Corp., 276 F.3d 1368, 1371 (Fed. Cir. 2002).

infringement suit within 45 days. 21 U.S.C. § 355(j)(5)(B)(iii). If the patent-holder initiates such a suit, "the FDA may not approve the ANDA until expiration of the patent, resolution of the suit, or thirty months after the patentee's receipt of notice, whichever is earlier." Andrx Pharm., 276 F.3d at 1371. Plaintiffs initiated this action on July 25, 2008.

II.

Defendants assert that the '068 and '003 patents are invalid because plaintiffs engaged in inequitable conduct in failing to disclose the copending '244 application to the examiners of the '068 and '003 applications. The burden of proving inequitable conduct lies with the infringing parties. Star Scientific, Inc. v. R.J. Reynolds Tobacco, Co., 537 F.3d 1368, 1365-66 (Fed. Cir. 2008). The infringing parties must prove by clear and convincing evidence that the patent applicant "(1) made an affirmative misrepresentation of material fact, failed to disclose material information, or submitted false material information, and (2) intended to deceive the [PTO]." Id. at 1366 (quoting Cargill, Inc. v. Canbra Foods, Ltd., 476 F.3d 1359, 1363 (Fed. Cir. 2007)) (internal quotations omitted). If the infringer meets this burden, the court then balances the equities to determine whether the entire patent should be held invalid. Id. Clear and convincing evidence is "evidence which produces in the mind of the trier of fact 'an abiding conviction that the truth of [the] factual contentions are "highly probable."' Buildex Inc. v. Kason Indus., Inc., 849 F.2d 1461,

1463 (Fed. Cir. 1988) (quoting Colorado v. New Mexico, 467 U.S. 310, 316 (1984)).

For the purposes of inequitable conduct, "information is material when a reasonable examiner would consider it important in deciding whether to allow the application to issue as a patent." Id. at 1367 (quoting Symantec Corp. v. Computer Assocs. Int'l, Inc., 522 F.3d 1279, 1297 (Fed. Cir. 2008)).[13] It is not necessary that the allegedly material reference would "conclusively decide the issue of patentability" so long as there is a "substantial likelihood" the examiner would consider the reference important. Li Second Family Ltd. Partnership v. Toshiba Corp., 231 F.3d 1373, 1379-80 (Fed. Cir. 2000). A reference is not material, however, if it is merely cumulative of other references the applicant disclosed. Digital Control, Inc. v. Charles Mach. Works, 437 F.3d 1309, 1319 (Fed. Cir. 2006).

With regard to copending applications, the Court of Appeals for the Federal Circuit ruled in July 1998 that one application can be material to a copending application with "considerable overlapping content in the specification and claims." Akron Polymer Container Corp. v. Exxel Container, Inc., 148 F.3d 1380, 1382 (Fed. Cir. 1998). The Court of Appeals had previously held in a non-precedential opinion that a later-filed

13. The Court of Appeals for the Federal Circuit is reconsidering en banc what information is material for the purposes of the inequitable conduct inquiry and the extent to which PTO rules influence that inquiry. Therasense, Inc. v. Becton, Dickson & Co., 374 Fed. App'x 35, 36 (Fed. Cir. 2010).

application can be material to an earlier-filed copending application even though the later application is not prior art to the earlier application. Id. (citing Akron Polymer Container Corp. v. Exxel Container, Inc., Nos. 95-1023, -1035, 1995 WL 620148, at *6, (Fed. Cir. Oct. 20, 1995) (non-precedential) (reported in table at 69 F.3d 554)). In 2003, the court concluded that a rejection made by one examiner "reviewing a substantially similar claim" is material to a copending application before a different examiner. Dayco Prods., Inc. v. Total Containment, Inc., 329 F.3d 1358, 1367-68 (Fed. Cir. 2003).

Because direct evidence of a party's intent to deceive the PTO will rarely be available, an infringing party may prove intent by circumstantial evidence. Star Scientific, 537 F.3d at 1366. However, the infringer may not prove intent merely by identifying a material reference not disclosed to the PTO. That party must also show a "deliberate decision" to withhold that reference. Id. An intent to deceive requires a greater showing of culpability than gross negligence. Kingsdown Med. Consultants, Ltd. v. Hollister, Inc., 863 F.2d 867, 876 (Fed. Cir. 1988). Moreover, an intent to deceive must "be the single most reasonable inference able to be drawn from the evidence to meet the clear and convincing standard." Star Scientific, 537 F.3d at 1366.

We find that defendants have proven by clear and convincing evidence that the '244 application was material to the '068 and '003 applications. Dr. Heber and both plaintiffs' and

defendants' expert witnesses testified that the compound cinacalcet, described in claim 5 of the '244 patent, is a species within the genus of compounds described in claim 7 of the '068 patent. It was well-established in 1997 and 1998 when the majority of the disclosure decisions in the '068 and '003 prosecutions were being made that an earlier-granted patent for a species compound could form the basis of an obvious-type double patenting rejection for a later application claiming a genus embracing that species. In re Berg, 140 F.3d 1428, 1431-33 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 1053 (Fed. Cir. 1993). We accept the unrebutted testimony of defendants' expert, Dr. Joseph Weinstock, that representative and non-representative species compounds claimed in the '244 patent fall within the genera claimed in the '068 and '003 patents' representative claims.

Thus, there is a "substantial likelihood" that a reasonable examiner considering the genus compound claims in the '068 and '003 applications would have deemed it important to know that an application claiming species compounds was also pending. Li Second Family, 231 F.3d at 1379; Akron Polymer, 148 F.3d at 1382. These examiners would have considered it important to consider the anticipation and obviousness rejections the '244 examiner issued after reviewing the prior art. This is especially true because, as the patent committee recognized, some of the prior art cited by the '244 examiner was also prior art to the '068 patent. Due to the inherent relationship between a

genus of compounds and species within that genus, the '068 and '003 examiners, it was important for the examiners to know that (1) an application had been filed claiming certain species within the genus of those two applications, and (2) a fellow examiner considered claims to those species obvious or anticipated.

We now turn to the question of whether defendants have established by clear and convincing evidence that the patent committee or any member of it acted with an intent to deceive in failing to advise the '068 and '003 examiners of the '244 application. Star Scientific, 537 F.3d at 1366. Defendants argue that the circumstantial evidence surrounding the patent committee's non-disclosure demonstrates intent. They submit that the patent committee knew that the longest patent term available on the '244 application was 20 years from filing since it was filed after June 7, 1995. In contrast, the '068 and '003 applications would receive the longer of 17 years from issuance or 20 years from filing since they were filed before June 8, 1995. Thus, if the prosecution of the '068 and '003 applications lasted longer than three years from filing of the '244, plaintiffs could extend patent protection to the genus of compounds beyond patent protection to the species compounds.

Defendants observe that at the time the patent committee disclosed the '244 application to the '068 and '003 examiners, the patent committee had already confronted double patenting rejections from the '068 and '146 examiners over other copending applications. Defendants are correct in noting that the patent committee recognized the related nature of the

applications as evidenced by disclosure of the '244 application. Defendants argue that the '068 and '003 examiners would have issued an obviousness-type double patenting rejection had they learned of the '244 application. Defendants also posit that by March 1998, when the one-way disclosure was made, the patent committee could foresee that the '068 and '003 prosecutions would extend beyond October 1998. Accordingly, the patent committee could foresee that patents resulting from the '068 and '003 applications would receive terms of seventeen years from the date of issue and thus extend beyond October 2015, when the expected '244 patent (which would have a twenty year term from the date of the filing of the application) would expire. Defendants attach special significance to the patent committee filing a CPA in the '244 application in May 1998 after receiving a notice of allowance for the '244 application. They contend the patent committee filed the CPA to avoid the '244 application issuing as a patent, which unquestionably would have to be disclosed to '068 and '003 examiners and which would anticipate the claims to the genera in those applications. While these circumstances may arouse suspicion, there is other evidence to be considered.

In 1998, the "prior art" that could disqualify an applicant from receiving a patent included an invention known or used by others in this country, or patented, or described in a printed publication before the applicant's invention; an invention patented or described in a printed publication more than one year prior to the patent application; and an invention described in a patent granted on another's patent application

filed "before the invention thereof by the applicant for patent." 35 U.S.C. § 102 (a)-(b),(e) (2000).[14] By 1998, the Court of Appeals for the Federal Circuit had held in a non-precedential 1995 opinion that a later-filed copending application could be material even though it was not prior art. Akron Polymer, 1995 WL 620148, at *6. The parties have not directed the court to any precedential opinion describing a duty to disclose later-filed copending applications until the Court of Appeals restated its 1995 Akron Polymer holding in a July 1998 opinion in a subsequent appeal of the same case. 148 F.3d at 1382. The 1995 Akron Polymer opinion does not cite any earlier case law for the proposition that a later-filed copending application is material. 1995 WL 620148, at *6.

Drs. Heber and Ungemach testified that the '244 application need not be disclosed to the '068 examiner because it was not prior art to the '068 application. Dr. Ungemach testified he formed that opinion during the prosecution because the '244 was a "selection" invention, which is, a species within another patent's genus. This explains why the patent committee would disclose the earlier-filed '068, '003, and '146 applications during prosecution of the later-filed '244 application but not the other way around. The patent committee may have reasonably believed that it was not required to disclose rejections issued in related prosecutions or copending

14. This version of § 102 had been in effect since 1975. See An Act to Carry into Effect Certain Provisions of the Patent Cooperation Treaty, and for Other Purposes, Pub. L. No. 94-131, § 5, 89 Stat. 685 (1975) (amending subsection (e)).

applications that were not prior art, including later-filed copending patent applications. As explained above, this view of "material information" is not accurate now and was incorrect even in 1998, but it is certainly plausible that the patent committee misunderstood the precise scope of its duty to disclose copending applications or rejections in related applications as more thoroughly explained by later case law. Dayco, 329 F.3d at 1368[15]; Akron Polymer, 148 F.3d at 1383-84. The law is clear that even gross negligence does not equate with intent to deceive. Kingsdown Med. Consultants, 863 F.2d at 876.

Even if, as defendants suggest, Drs. Heber and Ungemach's explanation about the '244 application's prior art status is a hindsight justification, the court would still find other conduct by the patent committee during prosecution is inconsistent with the intent to deceive. Most significantly, the patent committee did disclose the '068, '003, and '146 applications to the '244 examiner in May 1998. As the Court of Appeals for the Federal Circuit has noted, a one-way disclosure among copending applications points away from an intent to deceive. Akron Polymer, 148 F.3d at 1383-84. Moreover, when the '244 examiner issued anticipation and obviousness rejections based on prior art, the patent committee disclosed many of those

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15. Although Dayco was not decided until 2003, the Court of Appeals for the Federal Circuit found that its opinion in that case did not create a new obligation to disclose the opinions of examiners considering related copending applications. In Dayco, the Court of Appeals applied that duty to a patent claiming priority to a 1989 application. See McKesson Info. Solutions, Inc. v. Bridge Medical, Inc., 487 F.3d 897, 922-23 (Fed. Cir. 2007).

same references to the '068 examiner as prior art. The letter the patent committee sent to the '244 examiner on June 5, 1997 enclosing the prior art references stated that those references were cited by an examiner considering "a related application." Acknowledgment of a "related application" and the disclosure of potentially anticipatory prior art are flatly at odds with an intent to deceive.[16] The court finds that an intent to deceive is not the single most reasonable inference to be drawn from all the evidence. Star Scientific, 537 F.3d at 1366.

Defendants have a heavy burden. They have not proven by clear and convincing evidence that the patent committee, any of its members, or any inventor engaged in inequitable conduct in connection with the '068 or '003 patents.

III.

Defendants also argue that the court should invalidate the '068 and '003 patents for obviousness-type double patenting over the '244 patent. Obviousness-type double patenting is a judicially-created doctrine intended to prevent parties from obtaining separate patents on inventions "so alike" that allowing both to stand would effectively confer two distinct patent terms. Pericone v. Medicus Pharm. Corp., 432 F.3d 1368, 1368-69 (Fed. Cir. 2005). This doctrine ensures that an invention receives only one patent term by "prohibiting a party from obtaining an extension of the right to exclude through claims in a *later*

16. The court has considered the wording differences between the draft CPA disclosing the '068, '003, and '146 applications and the final version submitted to the PTO. Those differences are inconsequential.

patent that are not patentably distinct from claims in a commonly owned *earlier* patent." Eli Lilly & Co. v. Barr Labs., Inc., 251 F.3d 955, 967 (Fed. Cir. 2001) (emphasis supplied). This long-standing legal principle is designed "to prevent unjustified timewise extension of the right to exclude granted by a patent no matter how the extension is brought about." In re Schneller, 397 F.2d 350, 354 (C.C.P.A. 1968). When inquiring whether obviousness-type double patenting has occurred, the court considers the claims in the earlier patent and the later patent and determines the differences. Pfizer, Inc. v. Teva Pharm. USA, Inc., 518 F.3d 1353, 1363 (Fed. Cir. 2008). Next, the court "determines whether those differences render the claims patentably distinct." Id. At the second step of the inquiry, a later claim is "not patentably distinct from an earlier patent claim if the later claim is obvious over, or anticipated by, the earlier claim." Eli Lilly, 251 F.3d at 968. As with inequitable conduct, the party asserting this defense must prove double patenting by clear and convincing evidence. Symbol Tech., Inc. v. Opticon, Inc., 935 F.2d 1569, 1580 (Fed. Cir. 1991).

In the context of double patenting, an earlier patent claiming a large genus of pharmaceutical compounds does not preclude a later patent from claiming a species within that genus, so long as the species is novel, useful, and nonobvious. In re Kaplan, 789 F.2d 1574, 1577-80 (Fed. Cir. 1986); see Eli Lilly & Co. v. Zenith Goldline Pharm., Inc., 364 F. Supp. 2d 820, 909-10 (S.D. Ind. 2005). It is not surprising or controversial that either the same or a different inventor will improve upon

and attempt to patent a novel, useful, and nonobvious variation of a compound claimed by an earlier patent. Kaplan, 789 F.2d at 1578. Generally, the genus or "dominant" patent will expire while claims to the patentably distinct species or selection invention continue into the future. Id.

Defendants' double patenting argument turns on the peculiar facts of this case. Because of the change in patent terms as of June 8, 1995, the '068 and '003 patents on the genera compounds will expire *after* the later-filed and later-granted '244 patent on the species. Defendants argue that the '068 and '003 patents impermissibly extend patent protection to cinacalcet beyond the term granted by the '244 patent. In support of their position, defendants rely on Ex Parte Pfizer, a decision from the Board of Patent Appeals and Interferences. No. 2009-4106, 2010 WL 532133, at *14-*24 (B.P.A.I. Feb. 12, 2010).

In Ex Parte Pfizer, the PTO reexamined a patent granted on medicinal compounds used to treat erectile dysfunction. The reexamined patent, the '012 patent, was filed prior to June 8, 1995 and expired in October 2019, seventeen years from its issue. The '012 patent claimed a treatment for erectile dysfunction through oral administration of a genus of compounds. Pfizer also owned two other patents, the '511 and '945 patents, the applications for which were filed after June 7, 1995. The '511 and '945 patents claimed treatment of erectile dysfunction through administration, oral or otherwise, of particular species of compounds within the genus of the '012 patent. The '511 and

'945 species patents will expire October 2015, four years before the genus '012 patent will do so.

The Board of Patent Appeals and Interferences found that the '511 and '945 patents could serve as double patenting references for the '012 patent even though they issued later in time and expired earlier. The Board reasoned that the '012 patent prevented the public from practicing the art taught in the '511 and '945 patents beyond the terms of those two patents, which the Board argued is the purpose of the double patenting doctrine. In the Board's view, it is the patent term and not the issue date that determines whether a patent can be a double patenting reference. In a separate analysis, the Board found the oral administration claimed in the '012 patent obvious in light of the '511 and another Pfizer patent.

The court is not persuaded by the Board's reasoning. The Board argues that the double-patenting doctrine is designed to prevent unjust extension of a patent term, but its opinion makes no effort to explain why the shorter period must prevail. The opinion does not explain why a later-issued patent with a shorter term should be used to abridge the term of a valid, earlier-granted patent with a longer term.

In the case before the court, plaintiffs filed for the '068 application in 1994 and the '003 application in 1995. Then, after the change in patent term rules took effect, plaintiffs filed the '244 application. Although plaintiffs could not know when or if the PTO might grant each of the three patents, the possibility always existed that the '068 or '003 genera patents

would have longer terms than the '244 species patent. As discussed above, it is often the case that an inventor will improve upon an existing patent in novel, nonobvious ways and obtain a second, later patent on that improvement.[17] Normally, the later species patent term will expire *after* the earlier genus patent's term. Here, as in Pfizer, the legal changes to the patent terms, the timing of the applications, and the length of prosecution caused the species patent term to expire *before* the genus.

Had the patent law not been changed, the later-issued '244 patent would have extended beyond the '068 and '003 patent terms, as is typical with selection inventions. In such a case, we would proceed to determine whether the later species claims were patentably indistinct from the earlier-expiring genus claims. Here, even if the claims in the '244 patent were identical to those in the '068 or '003 patents, the '244 patent's term could not extend the patent protection to which plaintiffs were already entitled on the '068 and '003 patents. Accordingly, the court finds that the later-filed, later-issued '244 patent could not and did not create an "unjustified timewise extension" of the earlier-filed, earlier-issued '068 or '003 patents.

IV.

Defendants contend that the patent committee engaged in inequitable conduct in failing to disclose the '541 application

17. Of course, had the '244 patent issued before the '068 and '003 patents, the '244 patent would have anticipated and invalidated the '068 and '003 patents (or required common ownership and terminal disclaimers).

or patent to the '244 examiner during prosecution. As noted above, the '541 application was filed on September 28, 1995, issued as a patent on July 15, 1997, and expires September 28, 2015. Defendants argue that the '541 patent was material because it discloses a process for preparing a genus of compounds that includes cinacalcet as a species. It also states that calcimimetic compounds "have utility in treatment of hyperparathyroidism." Defendants contend that had the '244 examiner been aware of the '541 patent, the '244 examiner would have found the claims to cinacalcet anticipated.

Defendants assert that Dr. Van Wagenen, Dr. Ungemach, and Mr. Jensen breached their duty of candor by failing to disclose the '541 patent or application. Dr. Ungemach and Mr. Jensen worked for the patents' assignees. Thus, the court will infer that they were aware of the '541 prosecution and patent. In addition, the named inventor Dr. Van Wagenen testified he was aware of both the '541 and '244 patent prosecutions. Defendants have not adduced clear and convincing evidence, however, that Dr. Van Wagenen, Dr. Ungemach or Mr. Jensen withheld the '541 patent as a reference during the '244 prosecution with an intent to deceive the PTO.

Defendants contend that Drs. Heber and Warburg had a duty to inquire into the '541 patent's potential relevance even though it was prosecuted by another law firm. For the purposes of the inequitable conduct analysis, a party prosecuting a patent has no obligation to disclose art of which it is not aware or it should have been aware. Frazier v. Roessel Cine Photo Tech,

Inc., 417 F.3d 1230, 1238 (Fed. Cir. 2005); FMC Corp. v. Hennessy Indus., Inc., 836 F.2d 521, 526 n.6 (Fed. Cir. 1987). A party may not, however, "cultivate ignorance" in order to avoid obtaining actual knowledge of relevant prior art. FMC Corp., 836 F.2d at 526 n.6. This "duty to inquire" is triggered "when sufficient information [is] presented to the attorney to suggest the existence of specific information the materiality of which may be ascertained with reasonable inquiry." Brassler, U.S.A. I, L.P. v. Stryker Sales Corp., 267 F.3d 1370, 1382 (Fed. Cir. 2001).

Dr. Warburg and Dr. Heber worked for a firm other than the firm prosecuting the '541 patent, and there is no evidence that either attorney had knowledge of the '541 patent or application. Attempting to demonstrate such knowledge, defendants note that on June 5, 1997 Drs. Heber and Warburg disclosed two calcimimetic patents prosecuted by Trask, Britt & Rossa during the '068 prosecution. Neither of these patents was the '541 patent, which did not issue as a patent until more than a month later on July 15, 1997. Dr. Heber acknowledged in a deposition that he was aware of at least one NPS "process patent" pertaining to calcimimetic compounds granted by the PTO during his time at Lyon & Lyon. There is no evidence that Dr. Heber learned of this process patent during the '244 patent's prosecution or that the process patent of which he was aware was indeed the '541 patent. Consequently, defendants have not proven by clear and convincing evidence that Dr. Heber or Dr. Warburg

owed or breached a duty to inquire. Star Scientific, 537 F.3d at 1366.

Defendants have not established by clear and convincing evidence that plaintiffs engaged in inequitable conduct in relation to the '244 patent.

V.

Finally, defendants argue that the '541 patent, which discloses a genus of compounds, anticipated the '244 patent, which claims the species compound cinacalcet. As with inequitable conduct and double patenting, anticipation must be proven by clear and convincing evidence. Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings, 370 F.3d 1354, 1366 (Fed. Cir. 2003). In this analysis, the court must determine "whether one skilled in the art would reasonably understand or infer from the [prior art reference's] teaching that every claim element was disclosed in that single reference." Dayco Prods., Inc. v. Total Containment, Inc., 329 F.3d 1358, 1368 (Fed. Cir. 2003). The disclosure of the claim elements can be express or inherent, but the reference must permit one skilled in the art "to practice the subject matter based on the reference without undue experimentation." Sanofi-Synthelabo v. Apotex, Inc., 550 F.3d 1075, 1083 (Fed. Cir. 2008); Metabolite Labs., 370 F.3d at 1367. The anticipating reference also must disclose the elements "arranged as in the claim." Apotex, 550 F.3d at 1083 (quoting NetMoneyIN, Inc. v. VeriSign, Inc., 545 F.3d 1359, 1369 (Fed. Cir. 2008).

A patent to a genus of compounds anticipates a particular species if one skilled in the relevant art could "at once envisage" that species from a review of the patent. In re Petering, 301 F.2d 676, 681 (C.C.P.A. 1962). In Petering, the Court of Customs and Patent Appeals considered whether a prior art pharmaceutical patent claiming a genus of "perhaps even an infinite number of compounds" rendered obvious an application for a species compound. Id. The prior art patent claimed a general chemical structure with five locations at which numerous possible substituent compounds could attach. Id.

Even though the patent claimed an expansive number of compounds, the court looked to the specification's expressed preferences for certain substituents in certain positions on the compound. Id. at 681-82. The court found that in the total context of the patent, these expressed preferences defined a subclass of compounds that would be obvious to one skilled in the art because he or she could "at once envisage" each member of that subclass. It then evaluated whether each compound claimed in the application was obvious in light of the preferred subclass in the prior art patent. In a later case applying Petering, the court found that in the context of an anticipation analysis, the prior art "reference must clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without *any* need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference." In re Arkley, 455 F.2d 586, 587 (C.C.P.A. 1972) (emphasis in original).

A district court is required to construct properly all claims before comparing those claims to the prior art. Medichem, S.A. v. Rolabo, S.L., 353 F.3d 928, 933 (Fed. Cir. 2003). As noted above, claim 5 of the '244 patent teaches cinacalcet, and claim 26, by reference to claim 21, describes "[a] method of decreasing parathyroid hormone level in a patent to achieve a beneficial effect comprising the step of administering to said patient an effective amount of" cinacalcet.

Claim 1 of the '541 patent describes a process for producing billions and billions of compounds. As noted above, the genus of compounds described in claim 1 permits three right side substituents and twenty-two left side substituents. The genus permits between one and five left side substituents to be joined on each molecule. Of the myriad compounds within the genus, only fifteen are described as "preferred." One of the '541 patent's preferred compounds contains a trifluoromethyl group (F_3C) on the left side phenyl ring's meta position, as does cinacalcet. Significantly, each of the preferred compounds, including the two "most preferred," contains a 3-methoxyphenyl group on the right side. Cinacalcet, on the other hand, has a 1-napthyl group in that position.

Defendants' expert witness testified that one skilled in the art could at once envisage cinacalcet from the '541 patent's preferred compounds. Dr. Weinstock stated that one skilled in the relevant art could at once envisage each of the fifteen preferred left-side substituents with each of three

permitted right-side substituents to describe a total class of 45 preferred compounds.

We find this testimony unpersuasive. The '541 patent teaches a preference for 3-methoxyphenyl at the right end of the compound. None of the preferred compounds teaches 1-napthyl in that location. Defendants have not explained why one skilled in the art would ignore non-preferred left-side substituents, but would envisage compounds containing the two non-preferred right-side substituents. Dr. Weinstock defended this conclusion by arguing that claim 1 of the '541 patent embraces so many left-side substituents as to render the claim "meaningless" for one skilled in the art. However, Dr. Weinstock admitted under cross-examination that many of claim 1's left-side substituents are found in useful and profitable pharmaceutical products.

We find credible Dr. Paul Bartlett, plaintiffs' expert witness, who testified that the preferred left-side substituents are so diverse chemically, both in composition and placement on the phenyl ring, as to suggest that they were not especially significant to the inventors. According to Dr. Bartlett's testimony, this diversity increases the importance of the unchanging right-side substituent to one skilled in the art. Cinacalcet remains just one of the astronomical number of compounds the '541 patent's process could create. One skilled in the relevant art would not "at once envisage" cinacalcet from the '541 patent.

Accordingly, we find that the '541 patent does not anticipate claims 5 or 26 of the '244 patent.